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E D I T O R I A L

THE SURVIVAL OF PRIVATE EDUCATIONAL INSTITUTIONS

ALL schools and colleges are faced with exceedingly difficult problems which have arisen over the past several years by reason of many complex factors. The elementary schools are grossly overcrowded and understaffed because the willingness of our citizens to pay the costs of educational facilities has not matched the great surge of youngsters resulting from the increased birth rate of the last decade. Not only are physical facilities inadequate but there is a teacher shortage which approaches a national scandal, with little hope for relief in sight. This same pressure will soon hit the high schools with an impact which promises to cause even more serious results.

Colleges and universities, too, have their problems. State supported institutions, while presently the better off, can expect budgetary cuts as legislative bodies become economy-minded. Private institutions have had and have now the most difficult problems of all. They have been faced with rising costs, lowered enrollments and reduced income from investments and philanthropies.

Over the past several years it has become increasingly difficult to close the gap between income and expenses. Faculty salaries have lagged far behind the cost of living index and many of the best teachers have left colleges to join industry where they usually can expect an immediate and sizable increase in salary. Building and maintenance costs have trebled or quadrupled and every item which must be purchased has increased in price proportionately. Tuition fees have been raised until private colleges can go no higher without pricing themselves out of the market. Yet no college can expect to cover costs from tuition fees alone. In fact, it is not only impossible to do this and maintain a sound program, but it would violate all accreditation standards applied to our colleges.

Those who are able to make large gifts to educational institutions have become fewer and fewer since the advent of a tax structure which

is essentially confiscatory in the higher income brackets. Many businessmen, today, are forced to save desperately so that upon their death their estate can pay the estate taxes and manage to save the family business from being transferred to bank ownership and control.

Private colleges are faced with the almost certain need of broadening the base of their financial support in their long term planning. The contribution of every alumnus and friend is important, regardless of how small. The only other alternative is to cast their lot with other state institutions and ask for tax money as a means of support. There are those who give this problem superficial thought and suggest that state support is the only answer. Others who see the problem more intimately envision this solution as equivalent to selling one's birthright of freedom and independence and leading to the eventual destruction of the American way of life.

It is a trite but true saying "that he who controls the purse strings controls policy". In every country where higher education has been completely financed by the state it has been an easy matter for a dictator or a political party to control the university system and to select the faculty from "reliable" party followers. Thus has truth been concealed from the youth of such countries and true education and learning prostituted to the will of the party. We saw this in Germany under Hitler and it may be seen even today in a number of countries.

That this has not and does not happen here is not because Americans as a people are vastly different from others. We are free because we established and still maintain those institutions dedicated to freedom of thought and expression. These over the years have acted as the guardians of our liberties when there arose those who would deprive us of these great blessings. Private colleges and universities are in the advance guard of those institutions striving for the rights and freedom of the individual. In a sense the freedom of thought found in our state universities is guaranteed by our private colleges since the private institutions would be the first to speak out against any political dictation or repression in any place.

The college which has supported this journal financially for over one hundred and twenty-five years is now engaged in a campaign to enrich its permanent funds; this that its future may be more secure and its educational services continued. Those who read these pages can support both the cause of pharmaceutical education as well as

freedom in education by giving their help. The editor pays tribute to the institution which grants him an uncensored opportunity to speak the truth, as he sees it, on these pages. Those who enjoy reading this journal could support no more worthy cause than the college which gave this journal birth and has nurtured it over the years.

L. F. TICE



THE SILENT REVOLUTION*

By Theodore G. Klumpp,** M. D.

THE Philadelphia College of Pharmacy and Science celebrates its 132nd birthday today. It is, as you already know, the oldest school of pharmacy in the United States. In all of pharmacy and medicine there are not many institutions that are more venerable. Only five medical schools can claim a longer history than our College, and of these, the oldest was founded by Quakers, as was this. The American Medical Association came into being 26 years later. When the Philadelphia College of Pharmacy and Science was born, not one of the presently active pharmaceutical manufacturers nor cosmetic houses existed. But more important than mere longevity and survival is the fact that you were the only school of pharmacy in 1821 and you are still the leading school 132 years later. This proves that your ancestry has been good, and if I may be pardoned for saying so, it is also strong evidence that your contemporary Board of Trustees, Faculty and President are doing a superb job. This is true because a school, like any other living thing, moves either forward or backward. It does not stand still.

I suspect that I was asked to make this short talk because, like your President, I have been interested for a long time in the subject of longevity. After all, our College is the best example of longevity there is to be found in the entire realm of American Pharmacy. I have concerned myself with the silent social revolution that is happening in the United States before our as yet unseeing eyes. Fortunately, it is the best revolution possible and it couldn't have happened to a finer country. But all revolutions, good or bad, call for action, and this beneficent one is no exception. Unless we take steps to adjust our thinking and the whole pattern of our society to the changing state of affairs, this very good thing that is occurring may lead to serious maladjustments, discontent and unhappiness.

The revolution I have in mind was brought about by the scientists, the doctors, pharmacists, chemists, surgeons, public health

* Founders' Day Address, Philadelphia College of Pharmacy & Science, Philadelphia, Pennsylvania, February 23, 1953.

** President, Winthrop-Stearns, Inc.

workers, pharmacologists, pathologists, the medical schools, schools of pharmacy, and our Universities. Many of you may think that the atom bomb is the biggest thing that has happened in our generation. What I am talking about is, I believe, more important than the atom bomb because history has proved over and over again that constructive forces have had a more profound influence on man's development than those that are destructive. Despite the sad interludes, those lapses of destruction and killing, for which man must hang his head in shame, he has, nevertheless moved forward in a stream of steady progress. And grimly enough, sometimes from the ashes of fire and the sword have sprung our finest cities and our most noble works. Even now, from this great destructive atomic force that now seethes and smoulders in our midst may come some great good. Already atomic energy is being enlisted in the ranks of medical science and what its ultimate potential for good is, no one dares dream.

What I am talking about can be expressed in statistics, the most eloquent summation of which is in terms of our life expectancy which has moved upward from 49 years in 1900 to almost 68 in 1953. During the same period the death rate has similarly declined. In 1900, among any average group of 1000 persons, you could count on 17 dying that year. Today only 9 out of that same number will depart this world. Among infants the revolution is even more marked: at the turn of the century, 162 died out of every 1000 that survived birth, whereas today less than 30 succumb. Looking at it from another angle, we have seen the almost complete elimination of such one time killers as cholera, yellow fever, small pox and the plague, and such diseases as diphtheria, scarlet fever, typhoid fever, tetanus, rickets and Rocky Mountain spotted fever have lost their lethal terror. In half a century the greatest reaper of them all—pneumonia—has been defeated as witnessed by the fact that the death rate has declined from 152 per 100,000 to 12. Only 40 years ago, 1 of every 4 persons subjected to a major operation met his doom, whereas today only 1 in a hundred succumbs, and if that still seems high, let us remember that surgeons can now operate where the risk is great, whereas a few years ago they would not have dared touch many cases that now have been given at least a fighting chance to live. When I was in medical school, the idea of removing an entire lung for let us say cancer, was considered fantastic and in the realm of the impossible. Today, drugs and the perfection of surgical techniques have made lobectomies almost routine for expert surgeons. They are attacking the very citadel of

the human heart—and with amazing success too. I used to consider it quite an accomplishment to pass a tube into the stomach or the bronchi. My successors think nothing of slipping a tube into a vein and threading it safely back into the heart to find out what is happening to the stream of life in the very well from which it surges unceasingly day and night from the moment of birth until the end of time. Truly the constructive progress that has been achieved is nothing short of revolutionary. Compared with all the beneficent miracles of the healing arts, the atom bomb is but a frightening little pop gun that will stem the surge of man's progress no more than the firearms and cannons that came before it. In the early 17th century John Donne said, "The numbers of men slain now, since the invention of artillery are much less than before when the sword was the executioner." History often repeats itself and this observation of over 300 years ago may, we hope, find application to the circumstances existing today.

But let us consider more carefully some of the results of the silent revolution that is sweeping over us at such a swift pace. In 1860, 2.7% of the population or 848,920 persons were 65 and over, in 1900 it was 4.1% or 3,115,778. Since the turn of the century our population has doubled but the number of persons over 65 has quadrupled. Today there are approximately 12 million persons 65 years of age and over. By 1980, in only 27 years, it is anticipated that we will have twice that number. If the total population increases as expected, in 1980 one of every 7 persons living will be 65 years of age or over, and 2 of every 5 will be 45 years or over. In other words, in less than thirty years we may expect to have at least 66 million persons who are 45 and over and 24 million 65 and over. This means that we shall have more people over 45 years of age than the total number employed at the present time. Another factor of importance that is not as easily susceptible to statistical analysis, but is nevertheless clearly true, is that our older persons are healthier in body and mind than they used to be. There is every reason to believe that these advances will continue, with the result that in living longer we will also live even healthier lives in the future.

The age shift in our population promises to become one of the most important factors in influencing the entire economic and political structure of the nation. For one thing, if old folks are not content and their basic needs are not wisely met, they can act as a united group, the power of which has been already demonstrated in regional

tests. A bloc of some 20 million voters, joined by a few million more of those approaching 65 can very easily make their own political and economic decisions without much regard for the views of others. Under such circumstances the wisdom that is supposed to come with age may not be so clearly manifest to the rest of us. When Winston Churchill so truly said, "You can measure the civilization of a people by the way they treat their older folks," he was not thinking of a day when we might begin to wonder how the old folks are going to treat the rest of us.

With this in mind, I see no way of escaping the conclusion that the future must be considered from two distinct points of view: the "human side", and from the standpoint of the economics of the problem. The two must be reconciled or there will be trouble. Fortunately many students of the problem believe the two points of view can be harmonized.

What do our elders want and need? Basically they want and need the same things as the rest of us—happiness and a fair measure of security. Obviously the formula for happiness contains many and varying ingredients and there is no one prescription that will satisfy every need. But the experience of untold generations has shown that most human beings are not basically happy unless they have something useful to do, and this is particularly true of older individuals. It was Robert Burton who said, "Employment, which is nature's physician, is so essential to human happiness that indolence is justly considered as the mother of misery". Youth can loaf content with opiate dreams of future achievements. But as we grow older the realities of life are more clearly seen and less easily denied, and as we approach 50 and 60 we can no longer derive solace from the pipe dreams of future achievements. Age plays for real stakes not pastime. Older persons must have something to do, and it must be real. And the most real thing we have to sustain us in this life of ours is useful work. And yet, standing squarely in the way of this truth, is our system of compulsory retirement which, when it gained widespread acceptance, was looked upon as a great social advance. And a half century ago it was. But the old order changes. What served one generation well may not be best for the next. With your indulgence, I would like to discuss the implications of the silent revolution within the scope of work and retirement, and this is the principal message I bring today. To you students this may seem to be a remote topic to be considering at this point in your lives. With real

justification you can say that it is putting the cart before the horse. But I think it is something you ought to know about even now, for the progressively growing age of our population and what happens to it will influence your future and your practice of pharmacy far more than many of the things you learned in school. You will feel its great impact long before you are as old as I am, and you might as well start thinking about it now.

Retirement is a successful experience for those who have been wise and foresighted enough to plan for it. But what they have planned for is most often merely a different kind of occupation. It is sometimes euphemistically called a hobby, which is nothing more than work with the sting of need taken out of it. You are an intellectual group with diversities of interest enabling you to adapt yourselves to a different way of life with relative ease. Most of you have more things that you want to do than time in which to do them. But you represent only a very thin, small, upper crust in our social structure. Unfortunately, most persons fail to cultivate a secondary occupational interest, and even if they could they would rather continue with what they have been accustomed to doing. And there is reason to believe that it is biologically unsound to toss such individuals on the scrap heap before they are ready for it. For any living organism that has been accustomed to a set routine for 40 or 50 years can't suddenly be shaken from its orbit without untoward consequences. The very first purpose of our endocrine system is to guard the body against abrupt changes in its status quo. In old age this system does not function as efficiently as it once did. It is a biological fact that functions and living tissues that are not used decline and atrophy. Applied to longevity I believe it is also true that nature tends to eliminate those that have relinquished their functional usefulness. Atrophy of disuse, both physical and mental, is the most insidious and deadly poison known to man. The philosopher, Lord Bertrand Russell, now in his eightieth year, wrote, "Most of the men I have known who have retired from work have died of boredom shortly afterward. A man who has been active, even if he has thought throughout his life that a leisurely existence would be delightful, is apt to find life unbearable without some activity upon which to employ his faculties. I am convinced that survival is easier for those who can enjoy life, and that a man who has sufficient vitality to reach old age cannot be happy unless he is active."

Our society has been quite illogical and inconsistent in its attitude toward the older worker as far as compulsory retirement is concerned. On the one hand, it is apparent that we have no objection to electing and appointing older individuals to positions of the greatest responsibility in government, business and the professions. Indeed, oftentimes their careers are just starting at a time of life when society is systematically dumping others on the scrap heap.

It would appear then that as far as the rank and file of workers is concerned, we have little objection to the imposition of blind and unselective compulsory retirement rules which automatically eliminate those in the ranks who have reached the same age regardless of their fitness, ability, and contribution to the group for which they labor. But, if the premise is that individuals over 65 are not worth their keep, then least of all should we permit persons above those ages to occupy the top and critical positions in our social structure. If we acknowledge, as is certainly true, that some are, and some aren't fit and pulling their weight at those ages, then we should use our intelligence to devise methods of determining which are, and which aren't fit for all workers, not just the upper crust. Certainly a man isn't fit one day and unfit the next because one page of the calendar has been turned. As the great physiologist, Dr. A. J. Carlson, stated, "The physiologic age of the worker is not synonymous with his chronologic age, owing to the individual variables in heredity, mode of living, accidents, and sequela of disease".

At the present time our life expectancy is 67 years. As medical science progresses the life span may increase to limits hardly dreamed of. We might even look forward to the experience of an interesting person: His name was Christen Jacobsen Dragenberg. Dragenberg was a Dane who lived to be 146 years of age, from 1626 to 1772. He went to sea when he was 13, took part in the wars of three kings against Sweden, served many nations in merchant navies, when nearly 70 was taken prisoner by Algerian pirates, was sold as a slave, escaped slavery after fifteen years, and at the age of 84 again went to war against Sweden. At 111 he married a woman of 60, outlived her, proposed at 130 to several women but was rejected. Mastering his disappointment, he lived on for sixteen years. Described as being of impetuous temperament, he lived a life far from blameless, but in his last five years, from 141 to 146, exhibited a conduct described as "quite respectable". If one man can live a life as full as this, there is no reason why science cannot make it possible eventually for many

more of us to marry at 111, propose and *be accepted* at 130, and live to 146. In other words, I agree with George Bernard Shaw when he said, "It is a shame to waste such a wonderful thing as youth on youth".

We choose and select when we hire, and I see no reason why we can't do the same thing when we retire our workers. One of the best teachers it has been my privilege to know and an outstanding figure in public health work, Dr. Milton J. Rosenau, was retired from the Harvard faculty on the basis of a compulsory retirement rule. He moved to another university where the rules were not so blind and where perhaps they could not afford the luxury of scrapping their best brains by the calendar. He continued his inspiring teaching, which I can assure you could be emulated by very few others, and was subsequently elected President of the American Public Health Association. The story is told that as he lay on his deathbed, he cocked open one eye as he had a habit of doing, saw the pretty nurse standing before him, and spoke his last few words, "I feel I am taking a turn for the nurse."

From a sociological standpoint inflexible chronological retirement rules are a reflection on the state of our intelligence in solving what ought to be a simple problem. Whenever society adopts a rule that eliminates the fit with the unfit, destroys the good with the bad, or punishes the innocent with the wicked, it is not a good rule. Civilization progresses by changing rules of this kind. In an imperfect society human beings are pushed around as a faceless mob. But social progress may be measured in the last analysis by the degree of skill and discrimination with which society solves the *individual* problems of its members. I am afraid Winston Churchill had the right idea when he stated that we are still an immature civilization.

The argument has been advanced that we must clear out the older workers to make room for the younger men so that their progress upward in an organization will not be unduly stymied. On the face of it this line of reasoning appears to have some merit. But it is only another way of stating that there are more workers than there are jobs. During the war when there was a manpower shortage, no one was afraid that the old, the lame, the blind, and the halt were taking jobs away from younger and more able workers. At other times similar arguments have been applied against the employment of women in business, government, and the professions. Certainly there is no arbitrary age at which older workers begin to

repress the advancement of younger individuals. In a sense, every older individual higher on the ladder of advancement, whether he be 65, or 55, or 45, is holding a job that a younger individual aspires to and feels he can fill. That is always true, and it will be just as true if we force everyone to retire at 50 or even 45, as we will have to do by 1980, if we don't find a more logical way of reducing the disparity between jobs and workers.

Another view that is widely held is that older individuals become over-conservative, and to make progress we must eliminate these obstacles in the path of progress. Here again there are such wide variations in human reaction patterns that I don't see how one can logically draw generalizations that will fit individual cases. A leopard does not change his spots as he grows older; they merely become more distinctive. Certainly Bernard Baruch, 82 years of age; Arturo Toscanini, age 85; Herbert Hoover at 78; General MacArthur at 72; Grandma Moses at 92; and Carl Sandburg at 75 are no obstacles in the path of progress, and neither Alben Barclay nor Tommy Manville have become more conservative as they have grown older. As far as the great mass of jobs now subject to compulsory retirement are concerned, it makes no difference at all whether an individual grows more or less conservative. If individuals in key positions become too conservative with age, or even too reckless, as they sometimes do, to meet the best interests of the organization, a retirement board operating on a selective basis can function to correct this development, as well as any other that may arise.

From an economic standpoint is it a sound proposition to permit older workers to continue working so long as they are productive and desire to do so? As far as our national economy is concerned there seem to be a number of good reasons why it is so. First of all, we must keep in mind the fact that our national wealth, purchasing power, and standard of living, rests squarely on productivity. Our economic stream seems to flow best when we have the largest number adding something to it and dipping out a commensurate amount. When large numbers of the population are unemployed they are neither contributing nor, by the same token, are they in position to consume as much. In other words, the economic turn-over is at a low level.

If we did nothing about it and maintained present-day working standards and conditions, we might well be confronted with a potential labor surplus of over 30 million workers by 1980. Economic fore-

casting (not unlike election forecasting) is a hazardous undertaking, but he who approaches the task from the standpoint of a static economy in the United States is certainly going to be wrong.

With this in mind, we must allow in our estimates latitude for increased employment through the development of new industries. On the other hand, we are witnessing an unprecedented surge of interest in science, and its accomplishments are providing the pattern of a great socio-economic revolution. One of the major incentives of this scientific boom is the saving of time and labor, which in the end amount to the same thing. We must anticipate the continued introduction of new labor-saving devices, perhaps on a scale never dreamed of before. The first fruits of this golden age of science are only beginning to ripen. In the future they will come to maturity at an accelerated pace with respect to life and labor saving. The net effect of this may be against a substantial increase of man hours of available work in relation to man hours of available workers.

If we will employ one-fifth of the 24 million over 65 years of age which we will have by 1980, at, let us say, an average of \$2500. per annum, it will mean 12 billion dollars per year that they will earn for themselves and which load of support will be taken largely off the shoulders of younger workers themselves included, whether by taxes or direct contributions.

Let us look at it from another point of view. We are witnessing today a great groundswell of public sentiment in favor of State or Federal old age pensions for those over 65. A figure of \$100. a month has been prominently mentioned as an objective. By 1980 this could cost the country 28 billion 800 million dollars. When this sum is added to other welfare benefits that have already been, or have every promise of being adopted we are confronted with an astronomical figure, which statesmen such as Bernard Baruch declare we cannot and will not be able to afford. As Mr. Baruch put it in this connection, "We dare not undertake more than our economy can stand or we will defeat our own purpose". "We must get away from employment policies based on cold arithmetical averages and take advantage of the skills and judgment of older people. How hideous a mockery it would be if, as a result of advances in medicine, surgery, hygiene, and higher living standards, older people were left willing and able to work—but Society deprived them of something useful to do".

The added years that science has given man places a new and greater responsibility on all of us as we grow older. We must make

a greater effort to avoid the mental and physical atrophy of disuse to which I have referred. Many of the unpleasant characteristics of old age are due to the fact that those involved have given up, they have stopped trying, and stopped using their faculties to the fullest extent. Science has shown they have quit learning not because they couldn't help it, but because they chose to. They have lost sight of what Oliver Wendell Holmes said, "To be seventy years young is sometimes far more cheerful and hopeful than to be forty years old". And here is one of life's great paradoxes:

The quest and goal of labor is to win security, comfort, rest, freedom from worry, freedom from hard work, and freedom from the struggle. And yet the irony of it is that when a person finally and completely achieves such a goal he is through—and he might as well be dead. The essence of life is its struggle. Viewed in this light, mother nature is a hard woman. But she is wise and tells us in Robert Louis Stevenson's words, "To travel hopefully is better than to arrive".

I have tried to give you something to think about in terms of the good silent revolution that science is bringing about. Our institutions of learning have carried the torch that has shown the way. Through the long span of 132 years, the Philadelphia College of Pharmacy and Science has led the way in its own field of endeavor. On this birthday celebration may I offer my heartiest congratulations! May I say, as a physician that your school, our school, is old in years but young in spirit. My prognosis is for a long and useful life ahead with no signs of retirement.

INVESTIGATIONS ON HECTORITE*

By Martin Barr ** and Ivor Griffith ***

WHILE studying the properties of various clays, hectorite, a clay which has been reported in the geological literature but never pharmaceutically, was come upon. This paper is concerned with a preliminary study of the properties and possible pharmaceutical applications of this clay.

Introduction

The name hectorite was first applied by Cox in 1882 (1) to a "hydrated pyroxene mineral" from the serpentine rocks of the Dun Mountains of New Zealand, and it was listed by Dana (2) under the pyroxenes. Its identity, however, was never established, the name as proposed by Cox never gained acceptance, and in this meaning has fallen into complete misuse.

In 1936, Foshag and Woodford (3) described an interesting clay mineral from Hector, California. Stresse and Hofmann (4) later proposed the name hectorite for this clay mineral.

Hectorite is a member of the montmorillonite group of clays. It is closely related to bentonite, which has as its chief constituent montmorillonite. It is essentially the magnesium end member of this group, and the almost total absence of Al_2O_3 , the presence of essential Li_2O , and the dominance of F over OH have established hectorite as a distinct mineral species.

The hectorite used in this study occurs in the Mojave Desert near Hector, San Bernadino County, California.¹ It is a buff, white colored material. Analysis of this hectorite shows that it is a magnesium silicate containing some iron, calcium, sodium, potassium, titanium, lithium, fluorine, carbonate and water. The clay was ob-

* From the Pharmaceutical Research Laboratories, Philadelphia College of Pharmacy and Science. This work was conducted with the aid of a grant from Lederle Laboratories Division, American Cyanamid Company. Presented before the Pharmacy Subsection, American Association for the Advancement of Science, December 29, 1952, St. Louis.

** Associate Professor, Philadelphia College of Pharmacy and Science.

*** President, Philadelphia College of Pharmacy and Science.

1. Ward's Natural Science Establishment, Inc., Rochester, N. Y.

tained in rock-like pieces and was finely powdered before investigations were performed on it.²

Part I—pH of Hectorite Suspensions

Hectorite suspensions (1, 3, 5, 7.5, 10, 15, 20 and 25% w/w) were prepared by adding the hectorite in small quantities to the distilled water in a mechanical mixer.³ The total amount of hectorite required for each suspension was added, in divided portions, in exactly two minutes, and the suspensions were stirred at the same rate of speed for eight minutes more. Two hundred gram portions of each suspension were prepared and stored in 8-oz. wide-mouthed bottles.

The pH⁴ of the suspensions were determined at the time of preparation and one, three, seven, and fifteen days after preparation. All the suspensions were shaken in their respective containers for exactly fifteen seconds before the pH determinations were made.

The results of the pH determinations of the suspensions at the time of preparation are recorded in Table I. There were no significant changes in the pH determinations taken one, three, seven and fifteen days after preparation; therefore these values are not included.

TABLE I—pH OF HECTORITE SUSPENSIONS

% w/w Hectorite	pH
1	9.85
3	9.70
5	9.50
7.5	9.10
10	9.00
15	8.85
20	8.70
25	8.40
Distilled Water	6.20

Discussion—The pH of the hectorite suspensions were found to be in the alkaline range, the phenomenon responsible for this alkalinity probably being one of hydrolysis as in the case of bentonite

2. Micropulverizer, 0.010 Herring Bone Screen, Micro Pulverizing Co., Summit, N. J.

3. Hamilton-Beach Mixer, Model E, No. 4 speed.

(5). It is also interesting to note that the pH of these suspensions is approximately 0.5 pH units higher than those of bentonite suspensions of corresponding strength (5). It is also seen that the pH of aqueous suspensions of hectorite fall as the concentration of hectorite increases. This is typical of other montmorillonite clays (5-7).

Part II—Titration of Hectorite Suspensions

Aqueous hectorite suspensions (3, 5 and 7.5% w/w) were prepared using a procedure similar to that in Part I. Variable quantities of 2N HCl and 2N NaOH were added to one hundred grams of the suspensions in 8-oz. wide-mouthed bottles. The pH⁴ of the different suspensions was determined twenty-four hours after the addition of the acid and base. A control was run using distilled water in place of the hectorite suspensions.

The results of the titrations are recorded in Table II and Figure I.

TABLE II
TITRATION OF 100 GMS. HECTORITE SUSPENSIONS WITH
2N HCl AND 2N NaOH

Suspension Number	cc. Acid or Base Added		pH of Suspension			
	2N HCl	2N NaOH	0%	3%w/w	5%w/w	7.5%w/w
1	8.00	—	1.10	4.20	4.82	5.90
2	6.00	—	1.30	4.90	5.40	6.10
3	3.00	—	1.62	6.03	6.10	6.30
4	2.00	—	1.72	6.18	6.30	6.60
5	1.50	—	1.80	6.30	6.60	6.81
6	1.00	—	1.90	6.58	6.77	7.10
7	0.50	—	2.50	6.90	7.30	7.70
8	0.25	—	2.71	7.32	8.09	8.37
9	0.10	—	2.74	8.21	8.57	8.72
10	0.05	—	2.77	9.13	9.18	8.98
11	—	—	5.95	9.70	9.50	9.20
12	—	0.05	10.21	10.22	9.72	9.45
13	—	0.10	10.68	10.73	10.30	9.70
14	—	0.25	11.10	11.12	10.92	10.70
15	—	0.50	11.45	11.45	11.40	11.12
16	—	1.00	11.74	11.62	11.50	11.68
17	—	1.50	11.80	11.94	11.80	11.72
18	—	2.00	11.84	12.11	11.92	11.87
19	—	3.00	12.00	12.24	12.02	12.00
20	—	6.00	12.02	12.28	12.20	12.10
21	—	8.00	12.04	12.30	12.29	12.20

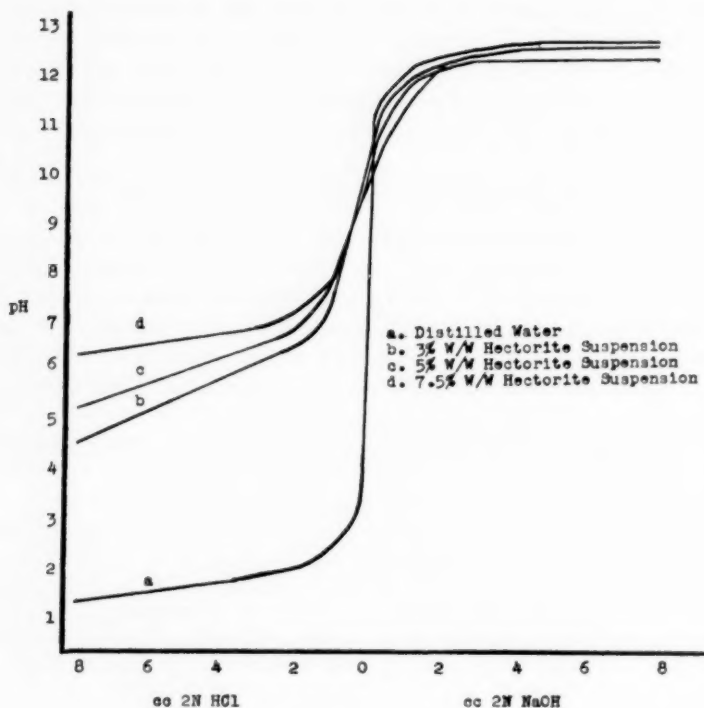


FIGURE 1.

TITRATION OF HECTORITE SUSPENSIONS WITH 2N HCl AND 2N NaOH.

Part III—Effect of pH on the Viscosity of Hecitorite Suspensions

One hundred gram suspensions of hectorite (3, 5 and 7.5% w/w) in distilled water were prepared as in Part I. Each suspension had a different pH produced by the addition of variable quantities of 2N HCl and 2N NaOH. The pH of the various suspensions was determined twenty-four hours after preparation.⁴

The viscosity of the various suspensions was determined twenty-four hours after their preparation in order to determine the effect

4. Leeds-Northrup pH Meter.

of pH on the viscosity of hectorite suspensions.⁵ Each suspension was shaken for thirty seconds before the viscosity determinations were made. The viscosity reading was made after ten rotations of the spindle of the viscometer in order to standardize the method.

The results of the study of the effect of pH on the viscosity of hectorite suspensions are recorded in Table III and Figure II.

TABLE III
EFFECT OF pH ON THE VISCOSITY OF HECTORITE SUSPENSIONS

Suspension No.	%w/w Hectorite	pH of Suspension	Viscosity (cps.)
A-1	3	1.20	3.0
A-2	3	4.00	2.6
A-3	3	6.10	3.8
A-4	3	7.05	5.6
A-5	3	7.40	8.0
A-6	3	9.70	16.0
A-7	3	10.40	46.0
A-8	3	12.20	6.0
B-1	5	1.30	4.3
B-2	5	4.75	3.8
B-3	5	6.25	3.2
B-4	5	7.25	17.6
B-5	5	9.50	52.0
B-6	5	10.30	57.0
B-7	5	11.10	42.0
B-8	5	12.20	6.1
C-1	7.5	1.05	4.9
C-2	7.5	5.80	4.2
C-3	7.5	7.10	4.4
C-4	7.5	8.35	57.0
C-5	7.5	8.90	81.0
C-6	7.5	9.20	412.0
C-7	7.5	10.65	140.0
C-8	7.5	12.10	8.4

Discussion—It is seen that the pH of hectorite suspensions markedly influences their viscosities. Maximum viscosities were observed in the range of pH 9-11. In the acid range, effervescence of the hectorite suspensions was observed. This is due to the activity of hydrogen ions on the carbonate in the hectorite. These suspensions, as a result of this incompatibility, have very low viscosities. The result of the effect of pH on the viscosities of hectorite

5. Brookfield Synchro-Lectric Viscometer, Multi-Speed Model LVF. All readings made at 60 r.p.m.

suspensions is somewhat similar to its effect on bentonite suspensions (8).

It was very difficult to measure the viscosities of the hectorite suspensions. This is because of the property of thixotropy which clays of the montmorillonite class possess. In an attempt to obtain as uniform readings as possible, the procedure previously mentioned for the measurement of the viscosities was utilized.

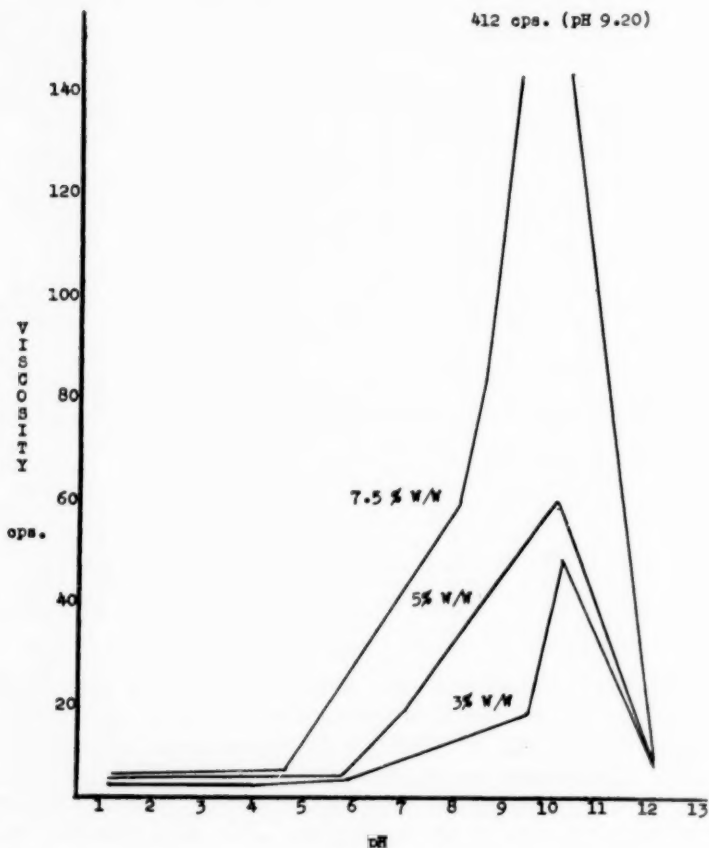


FIGURE II.

EFFECT OF pH ON VISCOSITY OF HECTORITE SUSPENSIONS.

Part IV—Comparison of Viscosities of Hectorite and Bentonite Suspensions

In order to determine the comparative viscosities of hectorite and bentonite suspensions, 300 Gm. quantities of aqueous suspensions of the respective clays were prepared. Viscosity measurements were made twenty-four hours after preparation of the suspensions using the method described in Part III.

The results of the study of the comparative viscosities of hectorite and bentonite suspensions are recorded in Table IV.

TABLE IV—VISCOSITIES OF HECTORITE AND BENTONITE SUSPENSIONS

% w/w Clay	Viscosity (cps.)	
	Hectorite	Bentonite
1	3.6	2.6
3	11.1	30.6
5	52.6	127.5
7.5	412.0	532.0
10	1540.0	2970.0

Discussion—It is noted that aqueous bentonite suspensions have a greater viscosity than hectorite suspensions of corresponding strength. Measurements of viscosity became increasingly difficult to perform as the concentrations of the clays were increased.

Part V—Effect of pH on Sedimentation of Hectorite Suspensions

Aqueous suspensions of hectorite (3, 5 and 7.5% w/w) were prepared and the pH adjusted to different values by the addition of 2N HCl and 2N NaOH. In an effort to determine the effect of pH on sedimentation, the following procedure was carried out. One hundred cc. portions of the individual suspensions were poured into 100 cc. glass stoppered graduates. The suspensions were allowed to stand without disturbance and the percentage of supernatant was recorded at time intervals of 5, 10, 15 and 30 minutes, 1, 6 and 24 hours after preparation.

The results of the study of the effect of pH on the sedimentation of hectorite suspensions and on the sedimentation rate of these suspensions appear in Tables V and VI respectively.

TABLE V

EFFECT OF PH ON SEDIMENTATION OF HECTORITE SUSPENSIONS

	ph	% Supernatant per 100 cc. Suspension						
		5 Min.	10 Min.	15 Min.	30 Min.	1 Hr.	6 Hrs.	24 Hrs.
A-1	1.10	90	90	90	90	90	90	90
A-2	4.00	86	87	88	88	88	88	88
A-3	6.10	78	84	84	86	88	88	88
A-4	7.05	26	40	46	52	60	70	72
A-5	7.40	0	0	0	0	0	0	0
A-6	9.70	0	0	0	0	0	0	0
A-7	10.40	0	0	0	0	0	0	0
A-8	12.20	17	30	40	66	79	82	82
B-1	1.30	82	82	82	82	82	82	82
B-2	4.75	69	74	86	80	82	82	82
B-3	6.25	47	60	64	73	76	78	78
B-4	7.25	0	0	2	3	5	16	49
B-5	9.50	0	0	0	0	0	0.5	2.0
B-6	10.30	0	0	0	0	0	0	1.0
B-7	11.10	0	0	0	0	0	0.5	1.0
B-8	12.20	3	6	9	25	52	68	70
C-1	1.05	50	65	70	73	74	74	74
C-2	5.80	26	53	63	70	74	74	74
C-3	7.10	2	10	27	35	44	60	64
C-4	8.35	1	1	1.5	2	2	2	8
C-5	8.90	0	0	0	0	0	0	0
C-6	9.20	0	0	0	0	0	0	0
C-7	10.65	0	0	0	0	0	0	0
C-8	12.10	2	3	5	11	24	56	58

Discussion—The results indicate that in the acid range the total sedimentation is greater than in the alkaline ranges. There is either little or practically no sedimentation in the range pH 7-11. As the alkalinity is increased above pH 11, the total sedimentation once again increases.

Part VI—Hectorite as a Constituent of Ointment Bases

It was found that an ointment base of petrolatum-like consistency could be formed by using the following formula:

HECTORITE BASE

	% w/w
Hectorite	25.00
Glycerin	10.00
Methylparaben	0.15
Propylparaben	0.05
Distilled Water q.s. ad	100.00

TABLE VI
EFFECT OF pH ON SEDIMENTATION RATE OF HECTORITE SUSPENSIONS

	pH	Sedimentation Rate %						
		5 Min.	10 Min.	15 Min.	30 Min.	1 Hr.	6 Hrs.	24 Hrs.
A-1	1.10	100.00	100.00	100.00	100.00	100.00	100.00	100.00
A-2	4.00	92.72	98.86	100.00	100.00	100.00	100.00	100.00
A-3	6.10	88.64	95.45	97.72	100.00	100.00	100.00	100.00
A-4	7.05	36.11	55.55	63.88	72.22	83.33	97.19	100.00
A-5	7.40	—	—	—	—	—	—	—
A-6	9.70	—	—	—	—	—	—	—
A-7	10.40	—	—	—	—	—	—	—
A-8	12.20	20.73	36.59	48.78	80.49	96.34	100.00	100.00
B-1	1.30	100.00	100.00	100.00	100.00	100.00	100.00	100.00
B-2	4.75	84.15	90.24	92.68	97.56	100.00	100.00	100.00
B-3	6.25	60.26	76.92	82.05	93.59	97.44	100.00	100.00
B-4	2.25	00.00	00.00	4.08	6.12	10.20	32.65	100.00
B-5	9.50	—	—	—	—	—	25.00	100.00
B-6	10.30	—	—	—	—	—	—	100.00
B-7	11.10	—	—	—	—	—	50.00	100.00
B-8	12.20	4.26	8.57	12.86	35.71	74.28	97.14	100.00
C-1	1.05	67.57	87.84	94.59	98.65	100.00	100.00	100.00
C-2	5.80	35.13	71.62	85.13	94.59	100.00	100.00	100.00
C-3	7.10	3.13	15.62	42.19	54.69	68.75	93.75	100.00
C-4	8.35	12.5	12.5	18.75	25.00	25.00	25.00	100.00
C-5	8.90	—	—	—	—	—	—	—
C-6	9.20	—	—	—	—	—	—	—
C-7	10.65	—	—	—	—	—	—	—
C-8	12.10	3.44	5.16	8.60	18.97	43.45	96.55	100.00

The Hectorite Base, was prepared by adding the hectorite in small portions, to the glycerin and distilled water in which the parabens had been dissolved, in a mechanical mixer³ and stirred until a homogeneous preparation resulted. The glycerin serves as a humectant and the parabens as preservatives.

Ointments of sulfathiazole (5% w/w), ammoniated mercury (5% w/w) and phenol (2% w/w) were prepared using Hectorite Base as the vehicle with the usual pharmaceutical technique. An attempt was made to prepare an ointment containing boric acid, but the presence of carbonate in the hectorite produced an apparent incompatibility.

The prepared ointments were tested for their anti-bacterial activity using the F.D.A. cup-plate method (9). The organisms against which the ointments were tested were *S. typhosa* (U. S. D. A. strain), *S. aureus* (U. S. D. A. 209 strain) and *E. coli* (Levine strain). Ammoniated Mercury Ointment (U. S. P. XIV), Phenol Ointment (N. F. IX) and Sulfathiazole 5% in White Ointment (U. S. P. XIV) were included in the testing procedures.

The results of the bacteriological tests of the ointments are listed in Table V.

TABLE V—RESULTS OF BACTERIOLOGICAL TESTS ON HECTORITE BASE AND OINTMENTS

	<i>S. aureus</i> Zone of Inhibition mm.	<i>E. coli</i> Zone of Inhibition mm.	<i>S. typhosa</i> Zone of Inhibition mm.
5% Sulfathiazole (White Oint.)	0.0	0.0	0.0
5% Sulfathiazole (Hectorite Base)	0.0(4.0) ^a	0.0(12.0) ^{ab}	0.0(3.0) ^{ac}
5% Ammoniated Mercury (U. S. P. XIV)	4.0	2.0	3.0
5% Ammoniated Mercury (Hectorite Base)	6.0	4.0 ^b	6.0 ^c
2% Phenol (N. F. IX)	0.0	0.0	0.0
2% Phenol (Hectorite Base)	6.0	6.0 ^b	7.0 ^c
White Ointment	0.0	0.0	0.0
Hectorite Base	0.0	0.0 ^b	0.0 ^c

^a Zone of partial inhibition of growth.

^b Zone of apparent stimulation of growth.

^c Zone of apparent slight stimulation of growth.

Discussion—It is possible to take advantage of the swelling property of hectorite to prepare ointment bases from it. The base described is of a buff, white color, smooth, and with the consistency of petrolatum. It is naturally greaseless and is water washable.

The results of the bacteriological tests indicate that the tested drugs had greater antibacterial activity when incorporated in a Hectorite Base than when incorporated in fatty bases. The zones of inhibition obtained when these drugs were incorporated in Hectorite Base were similar to those obtained when incorporated in bases containing bentonite (10). There are no apparent advantages of hectorite over bentonite as a constituent of ointment bases except that hectorite produces bases having a buff white color as compared to the much darker color of bentonite bases.

The zones of apparent stimulation of growth in some of the ointments containing glycerin have been previously reported (10-11).

Part VII—Hectorite as a Suspending Agent

Suspensions of drugs commonly prescribed in pharmaceutical practice, such as precipitated sulfur, zinc oxide, precipitated chalk and talc, were prepared using hectorite and bentonite as suspending agents. It was generally found that hectorite was not as satisfactory a suspending agent as bentonite. Studies are under way in an attempt to improve the suspending properties of hectorite.

Summary

1. Hectorite, a montmorillonite clay closely related to bentonite, forms suspensions in water which are alkaline, the pH of these suspensions falling as the hectorite to water ratio increases.
2. Titration curves of hectorite suspensions (3, 5 and 7.5% w/w) are presented.
3. pH markedly influences the viscosities of hectorite suspensions. The hectorite used in this study is incompatible in the acid range due to presence of carbonate. Maximum viscosities were observed in the range pH 9-11.
4. Hectorite does not form suspensions as viscous as those formed with bentonite.
5. Hectorite exhibits the phenomenon of thixotropy which makes viscosity measurements difficult.
6. A formula for an ointment base utilizing hectorite is presented. Ointments of sulfathiazole, ammoniated mercury and phenol prepared with it give longer zones of inhibition than when these drugs are incorporated in greasy bases.
7. There are no apparent advantages of hectorite over bentonite as a constituent of ointment bases except that hectorite produces a whiter base. Bases prepared with the hectorite used in this study are incompatible with acidic drugs such as boric acid.
8. Hectorite is inferior to bentonite as a suspending agent in the tests utilized.
9. It may be possible to alter the nature of hectorite to change its properties markedly.

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SELECTED ABSTRACTS

A Comparative Evaluation of Gantrisin and a Sulfapyrimidine Triple Mixture. Lehr, D. *Antibiotics & Chemotherapy* 3:71 (1953). The study reported by the author dealt with the investigation in man and animals of absorption, tissue distribution, and renal elimination of Gantrisin and the sulfapyrimidine triple mixture, sulfadiazine, sulfamerazine, and sulfamethazine (equal partial amounts). *In vitro* antibacterial studies were also performed.

The results of this study showed that the triple mixture was distinctly superior to Gantrisin in the blood levels attained and in the penetration through the hematocephalic barrier. However, Gantrisin had the advantage of substantially higher urine concentrations and slightly lower values for acetylation. The blood levels for the triple mixture were twice that of Gantrisin in some cases on maintenance dosage. The concentration of Gantrisin in the spinal fluid was less than 10 per cent of the concentration in the blood while that for the triple mixture was 54 per cent and for sulfacetimide was 100 per cent. On the other hand, the urine concentrations of Gantrisin were many times those for the triple mixture.

The bacterial spectrum, *in vitro*, and the degree of antibacterial activity was essentially the same for both Gantrisin and the triple mixture. Considerable differences in antibacterial activity between the two drugs were found from time to time, but this variation was no greater than that between the sulfapyrimidine homologues themselves and it also followed no definite pattern.

The clinical application of a sulfonamide depends to a large degree upon its renal safety. The high solubility of Gantrisin and its acetylated product in the slightly acid and alkaline pH range of human urine is a great advantage of this compound. However, when the urine becomes more acid (pH 4.5-5.5), as it frequently does with acute systemic infections, the solubility drops off very rapidly. With the triple mixture the solubility declines very gradually as the pH is lowered. Thus it becomes very necessary to alkalinize the urine in order to avoid renal complications when Gantrisin is administered.

The evidence thus far would indicate that the incidence of side reactions with Gantrisin is about the same as that for the sulfapy-

rimidines. The production of sensitization is apparently dependent upon the height of tissue concentrations and is apparently additive for closely related compounds such as the sulfapyrimidines.

The author concluded that the triple mixture of sulfapyrimidines is the preparation of choice in the treatment of systemic infections because of the minimized danger of renal complications and the therapeutic efficacy. Gantrisin is the drug of choice for the treatment of urinary tract infections, since it permits the maintenance of high urine levels without exposing all tissues of the body to unnecessarily high drug concentrations.

The Therapeutic Use of Thiamine Hydrochloride in Dental Disorders. Bock, J. L. E. *U. S. A. F. Med. J.* 4:181 (1953). The use of thiamine hydrochloride in the treatment of a variety of dental disorders was discussed and case histories were given by the author.

Tic douloureux, trigeminal neuralgia, was treated in one patient with daily intramuscular injections of 100 mg. of thiamine hydrochloride. By the 10th day the pain was completely relieved. The author recommended that injections of thiamine be tried before surgery in the treatment of this condition. Surgery always leaves a permanent anesthesia. Thiamine was also found to be a valuable therapeutic and preventive agent in patients with fractures which may be, or may become complicated by shock, infection, or neurologic disturbances.

Herpes zoster lesions were cleared in two patients by the daily intraoral infiltration of 10 mg. of thiamine. In most of the patients treated for hypersensitive teeth a single intramuscular injection of 100 mg. of thiamine markedly reduced the sensitivity. In a few patients the condition was completely relieved.

Postoperative pain was also relieved by either intraoral infiltration or intramuscular injection of the vitamin. A period of exacerbation of the pain for a period of $\frac{1}{2}$ to 8 minutes following intraoral infiltration but not following intramuscular injection was observed. Paresthesia also responded to treatment with thiamine in 2 patients.

Dry socket is one of the most distressing complications which may occur following dental extractions. Relief of pain was obtained in all of the 50 patients treated within 15 to 30 minutes after the

intramuscular injection of 100 mg. of thiamine. Seven patients required a second injection and one patient a third injection for permanent relief. Subsequent healing of the socket also seemed to be accelerated. Trismus, a tonic spasm or rigidity of the muscles of mastication, was relieved in from 4½ to 25 minutes. The quickest response was obtained following intraoral injections but 10 mg. intraorally or 100 mg. intramuscularly both produced muscular relaxation and relief from pain.

Studies on the Absorption of Erythromycin. Josselyn, L. E., and Sylvester, J. C. *Antibiotics & Chemotherapy* 3:63 (1953). Efforts were made in this study to influence the absorption of erythromycin from the gastrointestinal tract by buffering the gastric contents and by protecting the antibiotic from the action of gastric secretion. Single doses of 200 mg. or 500 mg. of erythromycin were given to groups of 10 to 12 young adult volunteers and then the blood levels were determined.

Both the 200 mg. and the 500 mg. plain tablets gave higher blood levels when given before a meal than when given afterward. When the specially coated tablet was given there was no significant difference obtained whether given before or after a meal, but the blood levels were considerably higher than those obtained with the plain tablets. Also, the coated tablet provided a more prolonged elevation of blood level. However, there was a delayed initial absorption with the coated tablets. The median blood levels following the administration of a plain tablet with two tablespoonfuls of aluminum hydroxide gel were comparatively high, particularly when given after meals. Sodium citrate given along with a plain tablet before a meal produced no increase in the blood level of the antibiotic. The coated tablet, when given after meals, provided blood levels higher than those obtained with any of the other dosage forms.

Thus it would appear that erythromycin is probably partially destroyed by gastric secretion unless the antibiotic is protected or accompanied by a buffer. However, the antibiotic is readily absorbed from the gastrointestinal tract. Doses of 200 to 500 mg. will provide blood levels which are within the range of the *in vitro* sensitivity of most organisms susceptible to the antibiotic.

The Use of Succinylcholine in Electric Convulsion Therapy.

Adderley, D. J., and Hamilton, M. *Brit. Med. J.* No. 4803:195 (1953). The contraindications to convulsive therapy, in otherwise suitable patients, may be classified into two groups: those due to the convulsion itself, such as damage to bones, and those due to strain on the cardiovascular system, particularly heart failure and hypertension.

In a study of the use of the quick-acting muscle relaxant, succinylcholine, in electric convulsion therapy (ECT), it was found that succinylcholine produced a rise in blood pressure following an adequate relaxant dose. This rise was no greater than that produced by the ECT and was, therefore, generally unimportant. However, if autonomic ganglia blocking agents such as tetraethylammonium bromide or hexamethonium iodide were given this hypertension could be eliminated without reducing the effectiveness of the ECT. With the use of succinylcholine there could be produced a paralysis so complete that no muscular activity could be seen during the "convulsion". This eliminated all strain on the cardiovascular system from that aspect. Also, recovery from the relaxant effect of succinylcholine was very rapid, unlike that from the longer acting relaxants.

With the patient completely relaxed it was difficult to determine whether or not adequate electric convulsive doses had been given. Therefore, the authors developed a simple maneuver to detect the presence of the fit.

The dosage employed in most patients was 0.2 Gm. of sodium thiopental to produce unconsciousness and 1.5 cc. of a 5 per cent solution of succinylcholine to produce complete relaxation. The drugs were combined in the same syringe and injected intravenously.

Serum Levels Following Benzethacil Intramuscularly.

Fletcher, A. P., and Knappett, C. R. *Brit. Med. J.* No. 4803:188 (1953). Previously it had been found that the coupling of N,N'-dibenzylethylenediamine with penicillin resulted in a complex sparingly soluble in water. This complex, also called benzethacil, is therapeutically active when administered orally.

The authors studied the serum levels obtained following single intramuscular injections of 600,000 units of benzethacil in 19 volunteer male subjects. The serum penicillin levels were determined by

means of the *Sarcina lutea* plate technique of the FDA. The serum levels were recorded in tabular form. Four out of 5 determinations after 3 hours showed penicillin serum levels of 0.1 to 0.15 U/cc., after 72 hours 18 out of 19 showed levels of 0.03 to 0.1 U/cc., and even after 28 days 3 out of 5 determinations showed levels of more than 0.02 U/cc. Thus, the authors concluded that benzethacil gives sustained levels of serum penicillin following intramuscular injection considerably superior to any repository penicillin preparation yet developed. They felt that even if injections were spaced as far apart as 14 days a summation of dose effect might occur.

In five subjects the assayable penicillin levels appeared only intermittently. The authors felt that this was understandable because of the insoluble nature of the preparation and its long duration of action.

A number of promising clinical results have been reported. However, the long continued exposure of the patient to low and sometimes intermittent levels of penicillin from this preparation may result in a high incidence of sensitization reactions. Further study is necessary before this danger of sensitization can be fully determined.

The Administration of Terramycin Parenterally in Pediatric Use. Farley, W. J., and Konieczney, L. *J. Pediat.* 42:177 (1953). According to the authors intravenous terramycin has proven to be effective when given by subcutaneous clysis to infants and small children. Serum levels of the antibiotic were determined following single doses to confirm the fact that the antibiotic enters the blood stream rapidly and to help establish proper dosage regimen.

As a result of their studies the authors recommended that a concentration of 1 mg. per cc. be routinely employed. In average infections a dose of 10 mg. per Kg. of body weight should be given and repeated every 12 hours. In more serious infections doses of 20 to 25 mg. per Kg. every 8 to 12 hours may be necessary. They found that terramycin may be administered along with hyaluronidase without any evidence of incompatibility. Various vehicles were also used and found to be satisfactory, including physiological saline, dilute dextrose solution, one-sixth molar sodium lactate solution, and Darrow's solution.

The authors stated that a satisfactory response was obtained to therapy with terramycin by this route to a variety of common infections encountered in pediatric practice. They concluded that the administration of this broad-range antibiotic by hypodermoclysis is a useful and practical mode of therapy that can play a worthwhile role in the successful management of infectious diseases in childhood.

Therapy With Chloramphenicol in Measles. Cioffari, M. S. *Arch. Pediat.* 69:469 (1952). A series of 44 children with measles were treated with chloramphenicol palmitate in a custard-flavored suspension, but only 30 of the children returned for evaluation of the therapy. The author found that all of the 30 children were afebrile within 24 hours, 10 were afebrile in less than 48 hours, and 9 required 72 hours or longer for the temperature to return to normal.

The dosage employed was 50 mg. per Kg. per day in 4 to 6 divided doses. However, the author suggested that up to 100 mg. per day may have given better results. The antibiotic was well tolerated and found to be very palatable to the children. No toxic manifestations resulting from the drug were observed. During therapy or following therapy there was no evidence of the development of complications. In fact, complications in 3 patients, existing before therapy was instituted, cleared up rapidly with treatment. These three complications were cervical adenitis existing before the appearance of Koplik's spots, bilateral otitis media, and concomitant chickenpox.

Repository Penicillin Effective in the Treatment of Pinta. Kitchen, D. K. *Ann. N. Y. Acad. Sci.* 55:1186 (1952). Pinta, a non-venereal treponematosis, was treated in a series of 655 patients, all Mexican Indians. The clinical results obtained with the repository treatment with single injections of penicillin were exceptionally good and much superior to the results obtained with any other form of therapy ever employed, including heavy metals, aureomycin, chloramphenicol, and streptomycin.

The form of penicillin employed was microcrystalline procaine penicillin G gelled in oil and aluminum monostearate. All 16 patients with primary lesions were cured. Of the 151 patients with secondary

lesions 104 were cured and 47 were improved. Of 183 patients with late symptoms 74 were cured, 91 were improved and only 18 showed no improvement.

Since pinta is a disease of known etiology and since repository penicillin therapy has proven to be so effective in this series of patients the author was quite optimistically inclined to feel that the eradication of this disfiguring and stigmatizing disease is now a good possibility.

A Study of the Effect of Phosphorylated Hesperidin on Fertility. Chang, M. C., and Pincus, G. *Science* 117:274 (1953). The effect of phosphorylated hesperidin on fertility in rabbits and rats was studied by the authors in an effort to determine the way in which the drug functions as an antifertility factor. In one series of rabbits phosphorylated hesperidin was deposited in the Fallopian tube of impregnated rabbits at the time when the sperm should be penetrating the ovum. In a second series the sperm were suspended in 0.1 or 1 per cent phosphorylated hesperidin and then deposited in the vagina of female rabbits which had been induced to ovulate. In two series of rats, one group was given the compound intraperitoneally in a dose of 5 mg. per day and a second orally in a dose of 20 mg. per day 6 days before copulation and until the animals were sacrificed.

From the results obtained in these controlled experiments it seemed evident that phosphorylated hesperidin did not inhibit fertilization when deposited in the Fallopian tubes of rabbits at the time of sperm penetration, nor did it inhibit ovulation, implantation, or normal development of the embryo when administered intraperitoneally or orally to rats. The fertilizing capacity of rabbit sperm seemed to be inhibited somewhat by a concentration of 1 per cent phosphorylated hesperidin but the motility was not affected. However, it would seem highly improbable that such a high concentration of the drug would ever reach the testis or epididymis of an animal following oral or intraperitoneal administration.

Since there was such a great discrepancy between the results obtained in this work and that previously appearing in the literature, the authors tested the hyaluronidase inhibiting capacity of the phosphorylated hesperidin used. In this one phase of activity it proved to be potent.

The Treatment of Functional Amenorrhea. Barfield, W. E., and Greenblatt, R. B. *Am. J. Obst. & Gynec.* 64:1111 (1952). Functional amenorrhea is a symptom of endocrine imbalance. Always, before hormonal therapy is attempted, an attempt should be made to correct dietary deficiencies or excesses, as well as environmental or psychologic conflicts.

Whether or not the ovaries are present but with intact uterus and endometrium, bleeding can be induced in practically every patient by adequate estrogen and progesterone stimulation. When adequate intrinsic estrogens are present, withdrawal bleeding can be induced in most patients with an intact uterus and endometrium with progesterone therapy alone. This progesterone therapy may be given as progesterone parenterally in a dose of 10 mg. per day for 3 to 5 days, or orally in a dose of 30 mg. 3 times a day for 5 days, or as ethisterone in a dose of 10 mg. 3 times a day for 5 days. When intrinsic estrogen levels are low it is necessary to prime the endometrium with estrogens before progesterone will induce withdrawal bleeding. The estrogen in this case may be given as 1.25 mg. of estrone sulfate daily for 20 days.

A comparison was made in 328 courses of therapy given to 123 patients in which either ethisterone, 10 mg.; progesterone, 30 mg.; or a combination of estrogen, 1 mg. and progesterone, 30 mg. was given 3 times daily by ingestion for 5 consecutive days. These preparations were found to be practically equally effective in inducing withdrawal bleeding. However, the author stated that it is believed that the best results are obtained in the management of functional amenorrhea when cyclic administration of estrogen and progesterone is employed in a manner closely simulating the normal physiological process of the ovulatory cycle.

Studies in the Use of Lente Insulin, A New Long-Acting Form. Lawrence, R. D., and Oakley, W. *Brit. Med. J.* No. 4804:242 (1953). A new form of insulin developed by a Danish firm provides a prolonged action. It was found that very small quantities of zinc in the vicinity of 1 mg. per 1000 units was less soluble at the pH of the blood than protamine insulin, provided that phosphate and citrate ions were not present. By the use of an acetate buffer, rather than the long-used phosphate buffer to adjust the pH

of the insulin, in the presence of very small quantities of zinc an insoluble insulin preparation was formed. It was further found that the form of insulin, whether amorphous or crystalline, determined the length of action of the insulin. Activity from 12 to 36 hours was reportedly possible depending upon whether the insulin was amorphous, amorphous and crystalline, or pure crystalline. Based upon these findings 3 insulin preparations have been made available as "semi-lente", "lente", and "ultra-lente". These cannot be mixed with soluble insulin.

The authors used lente insulin on 11 adult diabetic patients all of whom were hospitalized. All of the patients had been previously standardized on soluble insulin, protamine zinc insulin, or globin insulin. The unitage of lente insulin employed was the same as the total unitage of the other insulins as standardized. The fasting blood sugar levels at 8 A. M., the noon level and the 6 P. M. blood levels were essentially comparable but by 9 P. M. the level obtained with lente insulin in most cases was considerably lower than that obtained with the other insulins. Thus the authors concluded that it would appear from this small series of patients that lente insulin is capable of controlling the blood sugar of moderately diabetic patients throughout the day without causing hypoglycemia during the night. They found that it exerts a short hypoglycemic action comparable with and equal to that of soluble insulin. It did not produce either local or general reactions and it appeared to be no more likely to produce hypoglycemic reactions than present insulin preparations.

The Duration of Activity of Trypsin Compounded in an Ointment Base. Loeb, H. G., and Farber, E. M. *Stanford Med. Bull.* 10:289 (1952). When crystalline trypsin is dissolved in a phosphate buffer at a pH of 7.0 it loses 75 per cent of its activity in about 3 hours. In an effort to overcome this limitation to its therapeutic usefulness, trypsin was dissolved in phosphate buffer at a pH of 7.1 and compounded into Carbowax 1500 so that 10 Gm. of the finished ointment contained 2 mg. of trypsin and 0.2 cc. of phosphate buffer. This ointment was divided into two portions and placed in green glass ointment jars. One jar was then stored at room temperature and the other at 4 C. These samples were then tested at intervals over a 94-day period for tryptic activity.

The tryptic activity was tested by dissolving one part of the ointment in 5 parts of phosphate buffer and then placing 0.1 cc. of this solution on a strip of unprocessed X-ray film. The film strip was incubated at 30 C. for 15, 30, or 45 minutes and then rinsed in cold water. The emulsion on the reverse side of the film was scraped off and the degree of digestion of the gelatin emulsion by the trypsin was estimated by means of a color densitometer.

By means of this semiquantitative method for testing the activity of trypsin it has been shown that the trypsin ointment loses about 50 per cent of its activity when stored at room temperature after a period of 6 to 13 days. Subsequent storing at room temperature for a period of at least 3 months showed no further appreciable loss of activity. Storage at 4 C. maintained the ointment without loss of activity for at least 3 months.

The Stabilization of Penicillin Solutions With Methenamine.

Hobbs, R. J., Livingstone, J. L., Reece, J., and Woodard, W. A. *J. Pharm. Pharmacol.* 4:911 (1952). Methenamine was the only one of some forty compounds tested which proved to have stabilizing effects on both buffered and unbuffered solutions of sodium benzylpenicillin. The optimum effects were obtained when methenamine and benzylpenicillin were present in equimolecular proportions in the presence of a citrate buffer.

Citrate buffered solutions (pH 7.0) of sodium benzylpenicillin with equimolecular proportions of methenamine, having an initial potency of 100,000 I. U. per cc., possessed 86 per cent of their original potency after 21 days storage at room temperature. Without methenamine only 6 per cent remained. A like solution, unbuffered but with an equimolecular proportion of methenamine, possessed 77 per cent of its original potency after 21 days storage at room temperature. Buffered solutions stored under refrigeration at 4 C. possessed 86 per cent of their original potency after 107 days storage when equimolecular concentrations of methenamine were added. Without the methenamine only 26 per cent remained.

In an attempt to find a vehicle which might be satisfactory for dispensing in hospital work 100,000 and 200,000 I. U. per cc. of sodium benzylpenicillin were dissolved in a vehicle composed of 0.5 per cent methenamine, 0.3 per cent sodium citrate, and 0.001 per cent

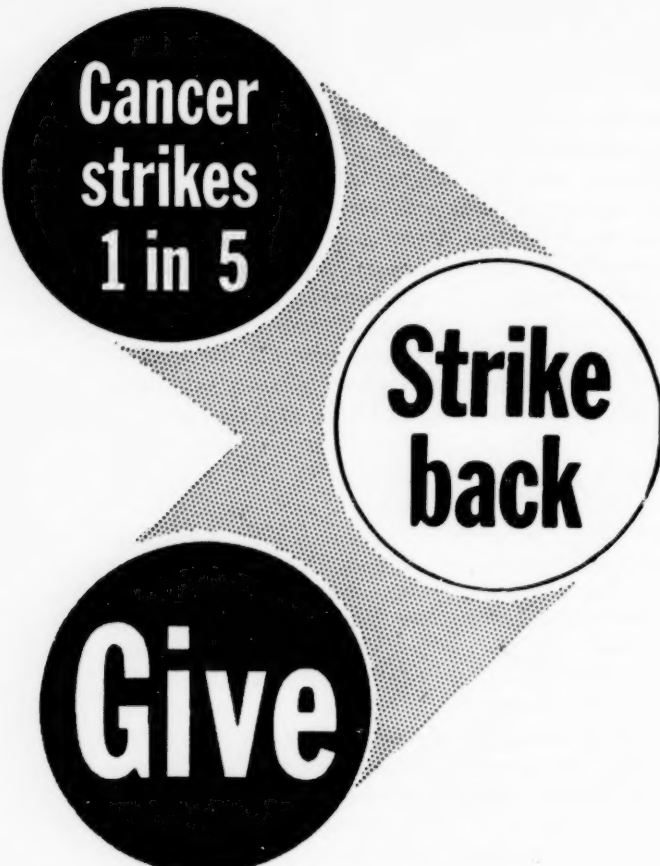
phenylmercuric nitrate. After 56 days storage under refrigeration (4 C.) the 100,000 unit and the 200,000 unit solution possessed 88 and 92 per cent, respectively, of its original potency. After 98 days storage 81 and 88 per cent, respectively, remained. When methenamine was not included in the vehicle only 16 per cent and a trace, respectively, remained after the 98 days of storage. Thus, when methenamine is included in the vehicle such a solution may be kept in a refrigerator for approximately twice as long.

The way methenamine acts in these solutions is not known. However, the pH of the solutions remains well above 6.0 throughout their life. Therefore, the liberation of formaldehyde is unlikely.

Dimercaprol in the Treatment of Toxicopathic Hepatitis Resulting from the Use of Fowler's Solution. Wade, H. J., and Frazer, E. S. *The Lancet* 1:269 (1953). A man had been under treatment with Fowler's Solution for dermatitis herpetiformis for a period of over one year. A total of about 80 grains of arsenic had been administered during that time. The dermatitis had been kept under control but it had not cleared.

The development of toxicopathic hepatitis resulted in hospitalization and the discontinuation of arsenic therapy. A high protein diet with vitamin supplements was begun and urinary arsenic levels were determined. These were found to be within normal levels after 3 weeks. It is known that it requires 10 to 14 days for uncombined arsenic to be completely excreted. Dimercaprol was then administered by intramuscular injection in doses of 3 mg. per Kg. of body weight every 4 hours for 48 hours and then twice a day. The urinary excretion of arsenic increased markedly. Therapy with dimercaprol was continued for 17 days, until excretory levels were insignificantly low. The increased excretion of arsenic following dimercaprol therapy confirmed previous observation that dimercaprol is capable of removing arsenic which has been combined with tissue proteins.

The patient improved subjectively and objectively following the therapy with dimercaprol. However, the authors felt that the patient's liver had sustained permanent damage from arsenic toxicity, as evidenced by diffuse fibrosis. There were no toxic effects from the dimercaprol but the patient had some pain at the sites of injection. He returned to work following discharge from the hospital.



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